The Relevance of Depressive Symptoms for Predicting Dementia is Greatest Close to Diagnosis

Investigating the Role of the Accumulation of Depressive Symptoms for the Risk of Dementia

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INTRO

- Depression is acknowledged as a late life risk factor for dementia[1], with potential pathways involving neuroinflammation[2], downstream vascular damage, and resilience to neurodegeneration
- Formal testing of relevance of depression across the life-course for later dementia is lacking
- Variation in depressive symptom trajectories over time and between individuals[3] impose challenges for modeling accumulation of exposure to depressive symptoms and subsequent risk propagation

We sought to explore the role of depressive symptom accumulation over time regarding dementia incidence in old age.

METHODS

1. Data:
- **3,717 participants (n=61 dementia cases)** of the Survey of Health, Ageing and Retirement in Europe (**SHARE**)[4]
- Waves 2 (**2006**) to 8 (**2020**)
- Eligibility criteria: age 65-70 at baseline, at least 3 measurements, no missing data

2. Measures:
- Depressive symptoms, **EURO-D**[5] scale
- Self-reported physician-diagnoses of **dementia**

3. Statistical Analysis
- Functional relevant life course exposure model (fRLM), with depressive symptoms as a function of time and incident dementia as outcome[6]
- Posterior probabilities were computed to assess relevance of exposure to depressive symptoms between time intervals

RESULTS

- Higher exposure to depressive symptoms over time was associated to higher dementia incidence (**OR [95% CI] = 3.66 [1.84-5.87]**)
- Highest relevance for age 72-75, close to diagnosis (Median [SD] age at diagnosis = 76 [3.26] years)

DISCUSSION

- Application of fRLM allowed to formally assess models of risk accumulation, suggesting highest relevance of depressive symptoms close to diagnosis
- Given the long prodromal stage of dementia, our findings suggest depressive symptoms as an early sign or accompanying symptom of dementia
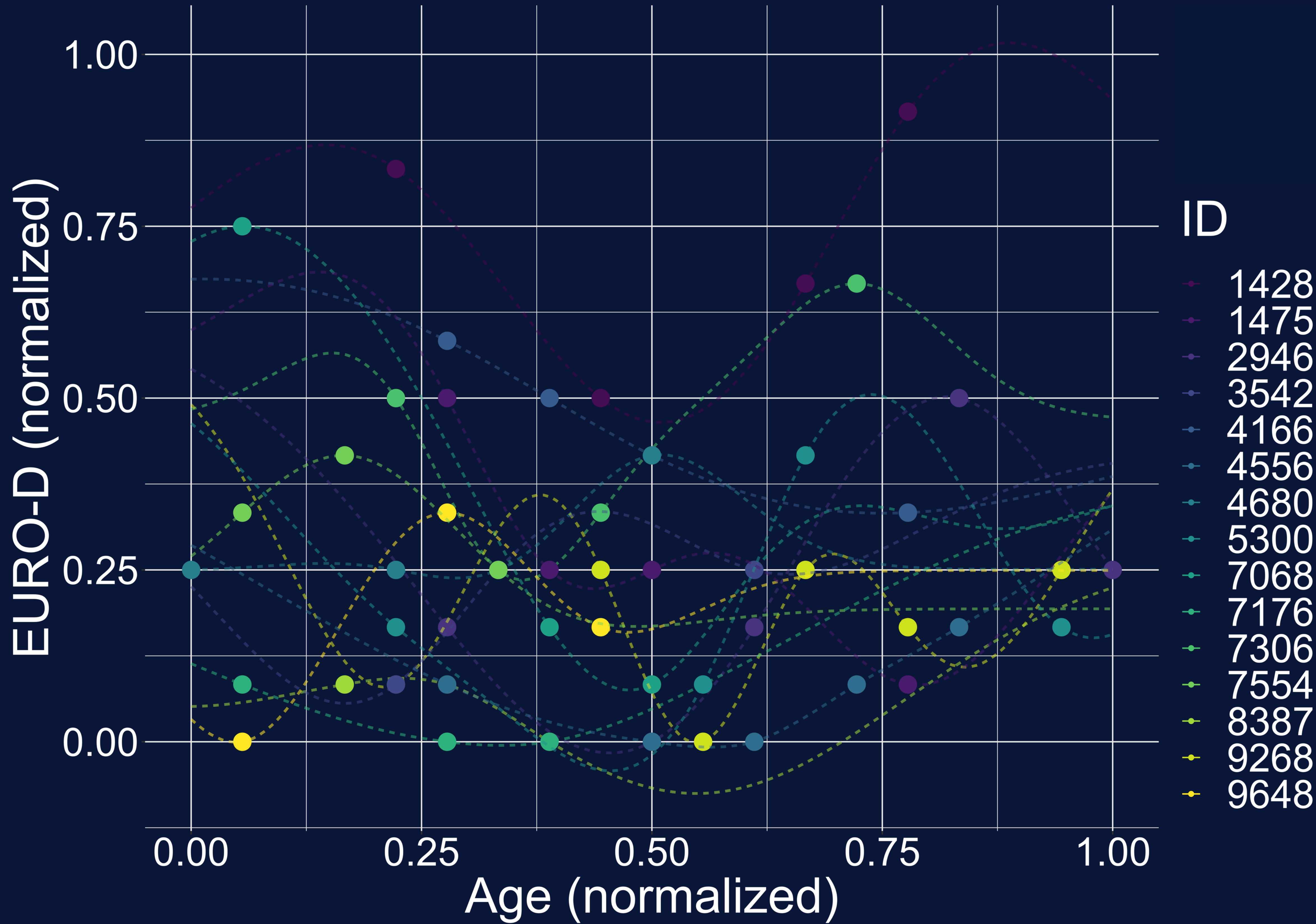

Figure 1. Observed (dots) and predicted (dotted lines) exposure to depressive symptoms across age for a subset of 15 participants. Age was normalized, with minimum age 65 and maximum age 83, EURO-D was normalized with minimum score 0 and maximum score 12.

Table 1. Baseline characteristics.

Characteristic	No Dementia	Dementia	P
n	3656	61	
Age (Mean, SD)	67.41 ± 1.7	67.59 ± 1.57	.390
Gender			
Female	2144	37	
Male	1512	24	.794
Education			
Tertiary	1056	13	
Upper 2nd	1209	17	
Lower 2nd	1391	31	.142
Income	1945.64 ± 1534.05	1682.45 ± 1539.67	.190
Physical activity			
Other	3454	51	
Never vigorous /moderate	202	10	.002
BMI	27.2 ± 4.32	26.87 ± 3.99	.530
SP health	3.03 ± 1.05	3.75 ± 1.06	.000
Living alone			
No	2159	35	
Yes	1497	26	.794

Note. Numbers refer to means ± standard deviations for continuous, n for categorical characteristics.
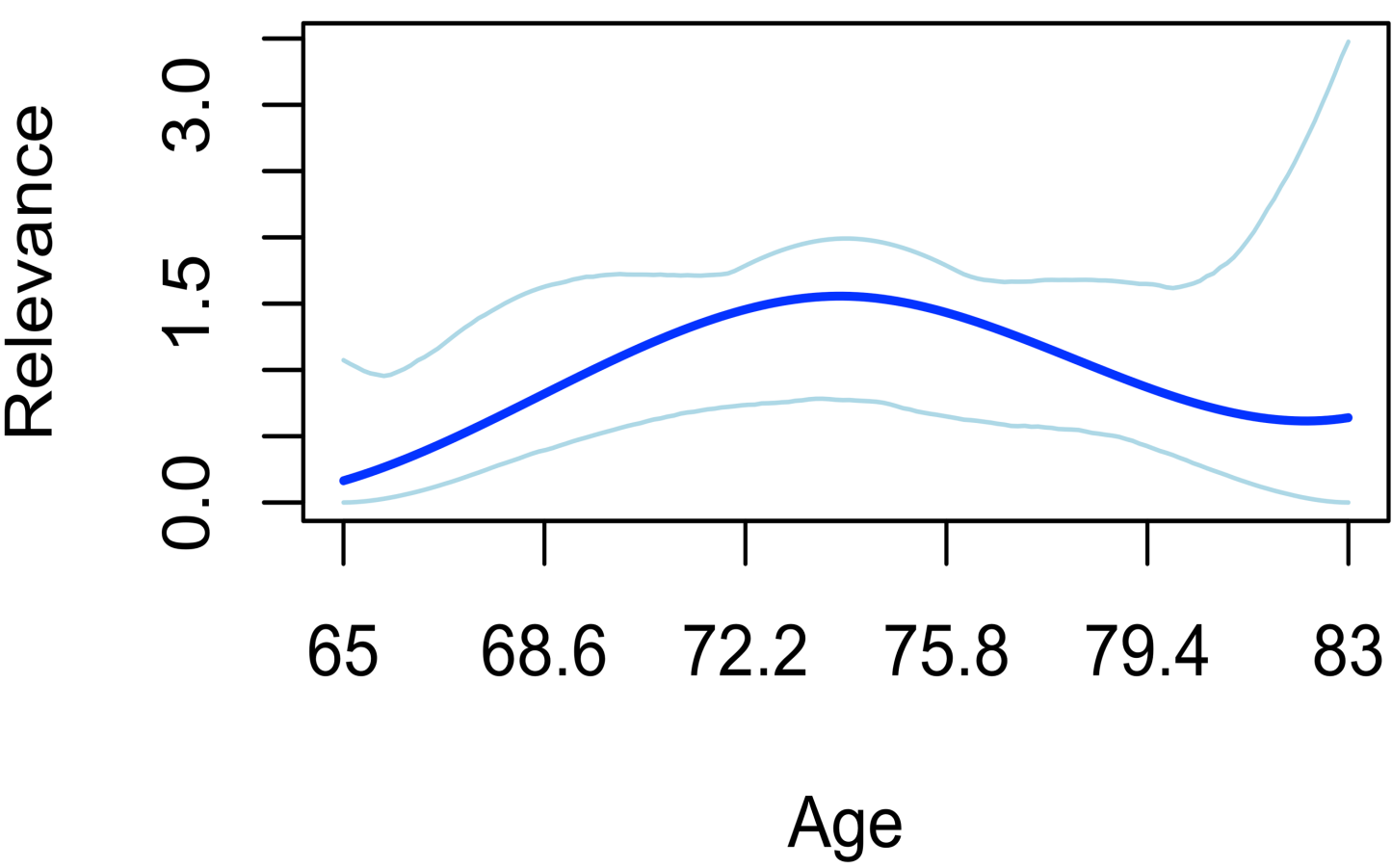

Figure 2. Relevance of exposure to depressive symptoms across age. The blue line indicates relevance with respect to incident dementia, the light blue lines indicate 95% CIs. Analyses was adjusted for Body Mass Index, physical activity, self-perceived health, cohabitation status, income, and household size at last measurement.

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